

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)



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| Applicant's or agent's file reference WBO-PCB-V130 | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/EP 03/50731 | International filing date (day/month/year) 17.10.2003 | Priority date (day/month/year) 18.10.2002 |
| International Patent Classification (IPC) or both national classification and IPC C12N15/82 | | |
| Applicant VIB vzw et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

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| Date of submission of the demand 06.05.2004 | Date of completion of this report 04.11.2004 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016 | Authorized Officer Maddox, A Telephone No. +31 70 340-2336  |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/50731**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

Description, Pages

1-19 as originally filed

Claims, Numbers

1-24 as originally filed

Drawings, Sheets

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority in written form.
☒ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/50731**

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-------|
| Novelty (N) | Yes: Claims | 1-14 |
| | No: Claims | 15-24 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-24 |
| Industrial applicability (IA) | Yes: Claims | 1-24 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.

1. The following documents are considered as relevant for the communication; the numbering will be adhered to in the in the rest of the procedure:

D1: Vander Mijnsbrugge, K., 1998, PhD Thesis, Univ. Gent
D2: Vander Mijnsbrugge, K., et al. 2000, Planta 211:502-509
D3: Hu W.-J., et al. 1999, Nature Biotechnology 17:808-812
D4: WO9839454
D5: EMBL Acc. No. AJ005803, 1 May 1998
D6: Gang, D.R., et al. 1999, J. Biol. Chem. 274:7516-7527
D7: WO0005350

2. **Novelty.**

- 2.1 The present application does not meet the requirements of Article 33(2) PCT, because the subject-matter of claims 15-24 is not novel.
- 2.2 The subject matter of claim 15 relates to a genetically modified plant having incorporated in its genome a recombinant nucleic acid encoding phenylcoumaran benzylic ether reductase(PCBER). D1 (cf. pages 43-91) discloses transgenic poplar plants transformed with the same sequence as the present application also disclosed in D5. In view of D5 and D6 (cf. p.7516 right col. para 2 and footnote 4; p.7518 left col. para. 2; p.7519 right col. last para. - p. 7520 right col.; page 7525) the person skilled in the art would have been aware that the sequences of D1 encode a protein with PCBER activity. D1 discloses both cosuppressed and antisense poplar lines identical to that of the application, having reduced lignin content. Figures 1,2, and 7 of the present application are also reproduced in D1 (cf. fig.3.14, fig.3.15 A, fig. 3.16). D2 discloses transgenic poplar plants downregulated for PCBER (cf. p.505 left col. lines 32-34 and fig 4E). Hence the subject matter of claim 15 lacks novelty with respect to D1 and D2. Claims 16-24 do not combine with claim 15 to form novel subject matter since the claimed features are also disclosed by or considered as inherent properties of the plants of D1 and D2.
- 2.3 Even in the absence of D1 and D2 the subject matter of claim 15 inherently lacks

novelty over wild type plants, since they also contain nucleic acids encoding PCBER. Claim 15 attempts to establish novelty over the wild type by inferring that the claimed subject matter is distinguished from the prior art by being "genetically modified" with "recombinant" nucleic acids, i.e. resulting from the process of genetically modifying plants with nucleic acids that result from a recombinant process. However a product, in this case a plant containing nucleic acids encoding PCBER, is not rendered novel merely by the fact that it is produced by the abovementioned process.

- 2.4 Claims 18-24 do not combine with claim 15 to represent novel subject matter over wild type plants (poplar). The features "increased (stem) biomass", "elevated CO₂ concentration", "lowered lignin content", and "increased resistance" are all relative terms the scope of which are not defined in the absence of a reference point. As a result there is no causal relationship between these effects and the PCBER encoding nucleic acid. It is evident that wild type plants falling within the scope of claim 15 also fall within the scope of claims 18-24, since they display natural variation in their (stem) biomass, lignin content, and pathogen resistance whereby some plants have increased or lower levels with regard to others. In addition all plants are naturally subjected to a variety of CO₂ concentrations, some higher than others. It follows from point 2.3 that the method for obtaining the plants in elevated CO₂ concentrations does not establish novelty thereof. Hence the subject matter of claims 15 and 18-24 is not novel within the meaning of Article 33(2) PCT.

3. Inventive Step.

- 3.1 Even if novelty could be established the present application does not meet the requirements of Article 33(3) PCT, because the subject-matter underlying claims 1-24 does not involve an inventive step within the meaning of this article.
- 3.2 The subject matter of claims 1, 13, and 15 concerns the modulation of plant biomass by repression of the activity of the enzyme PCBER, the plants also display reduced lignin content. Specifically stem biomass has been increased in transgenic poplar plants. D3 is regarded as the closest prior art with regard to inventive step. It discloses transgenic aspen (a species of poplar) plants having both reduced lignin content and increased stem biomass (cf. page 810 right col., table 1 and figure 4) using antisense 4-coumarate:coenzyme A ligase (4CL) constructs. The method and plants of the present application differ from those

disclosed in D3 in that repression of another enzyme (PCBER) leads to the same effect on biomass and lignin content. The problem underlying the claimed subject matter is to provide increases in plant biomass with decreased lignin content via the repression of alternative enzymes. Faced with this problem and with the knowledge from D1 (pages 43-91) that modulation of PCBER may be used to reduce lignin levels, the skilled person being aware from D5 and D6 that the downregulated PILa sequence of D1 encodes PCBER, the person skilled in the art would have adapted the teaching of D3 to repress PCBER to reduce lignin biosynthesis and increase biomass without exercising any inventive skill or ability beyond that expected of said person. The use of PCBER repression merely represents an arbitrary selection from a number of possible alternatives for reducing lignin content and hence increasing biomass. Since the reduction of lignin biosynthesis is also linked to increases in biomass in herbaceous plants (cf. D4 examples 5 and 6), the use of PCBER repression in non-woody plants for the same purpose, also follows plainly and logically from the prior art for the same reasons as mentioned above. Hence the subject matter of claims 1,13, and 15 lack inventive step within the meaning of Article 33(3) PCT..

- 3.3 Given that the sequence used in D1 (cf. fig.3.4A and D5) encodes the protein represented by SEQ ID NO:2 of the present application and the other effects of PCBER in D7 (cf. p.7 l.14 - p.8 l.6) the features of claims 2-12,14, and 16-24 do not combine with claims 1,13, or 15 to represent inventive subject matter, since they represent alternative embodiments that would have been arrived at by the skilled person during normal technical progress resulting from routine experimentation when faced with the technical problem mentioned above. The subject matter of claims 1-24 therefore does not meet the requirements of Article 33(3) PCT.

4. Clarity.

- 4.1 The subject-matter of claims 1,3-9,12-14,18,19,21 and 22 do not meet the requirements of Article 6 PCT.
- 4.2 The relative terms "modulate, repression, increase(d), lower(ed), higher, and elevated" used in claims 1,3-9,12-14,18-19 have no well-recognised meaning in

the absence of any reference point with which to compare the values of biomass, lignin or pathogen resistance. Due to the lack of reference point claims 18-22 lack a causal relationship between altering PCBER levels and biomass. Hypothetically plant X may already display higher biomass than plant Y. The expression of antisense PCBER for example in plant X may have no further effect on biomass, therefore falling outside the subject matter of invention, yet still within the scope of the claims. In addition claims 8,9,21 and 22 do not define a causal relationship between PCBER activity and either lignin content, or insect resistance. This leaves the reader in doubt as to the meaning of the technical features to which the claims refer, thereby rendering the definition of the subject-matter of said claims and those that combine with them unclear.

- 4.3 Claim 13 lacks an essential technical feature since it is not clear if the recombinant nucleic acid is expressed. Hence the claim does not meet the requirement of Article 6 PCT.

5. Description and Figures.

- 5.1 With regard to fig.1 the terminology in the description (cf. p.5) does not match that in the figure. This also applies to fig 9. The description (cf. p.6 ,p.7, example 5) mentions references to parts of fig.9 that are either not present in the figure (fig.2A,B as use on page 6; fig.9G,H,I as referred to on page 7 or 15) or are not used consistently (fig.C and F as used on page 7 and page16).